REMARKS

Claims 1-22 and 64-72 are pending in the application. In the Office Action dated August 11, 2004 (the "August Office Action"), claims 2-7, and 13-18 are withdrawn from consideration as belonging to a non-elected species, claims 1, 8-10, 12, 19-21, 64, 69 and 70 are rejected, and claims 11, 22, 65-68, 71 and 72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. In response to the August Office Action, Applicants filed an Amendment on November 10, 2004 (the "November 10 Amendment"), in which claims 1, 11, 12, 22, 64-65, 69, 70, and 72 were amended, and new claim 73 was added. In the Advisory Action dated February 8, 2005 (the "February 8 Advisory Action"), the Examiner indicated that the November 10 Amendment had not been entered. The Examiner contended that the amendments to claims 1 and 12 introduced new matter and raised new issues because the dependence of $R_{\text{target},k}$, and $R_{\text{off-target},k}$ on drug exposure level t_l was not explicitly recited. The Examiner also indicated that the prior art rejection based on Rine et al. was maintained and reiterated due to non-entry of the November 10 Amendment, but would have been overcome if the amendment had been entered. In response to the February 8 Advisory Action, Applicants filed an Amendment on April 11, 2005 (the "April 11 Amendment"), in which claims 1, 11, 12, 22, 65, 69, 70, and 72 were amended, and new claim 73 was added. The amendments were the same as those made in the November 10 Amendment except that claims 1 and 12 were amended to explicitly recite the dependence of $R_{\text{target},k}$, and $R_{\text{off-target},k}$ on drug exposure level t_l. In the Advisory Action dated June 1, 2005 (the "June 1 Advisory Action"), the Examiner indicated that the April 11 Amendment had not been entered. The Examiner contended that the proposed amendments raised two new issues: (1) the amendment to claim 72 caused an improper multiple dependency; and (2) the font sizes of subscripts in formulae in the amendments were smaller than the required font size. The Examiner also indicated that the prior art rejection based on Rine et al. was maintained and reiterated due to non-entry of the April 11 Amendment, but would have been overcome if the amendment had been entered. In response to the June 1 Advisory Action, Applicants submit the instant Amendment, in which claims 1, 11, 12, 22, 65, 69, 70, and 72 have been amended, and new claims 73-74 have been added. The amendments are the same as those made in the April 11 Amendment except that the improper multiple dependency has been removed from claim 72 by deleting the multiple

dependency in claim 72 and adding a new claim 74, and the font sizes of subscripts in formulae and equations have been increased to satisfy the requirements regarding font sizes. These amendments are proper and place the claims in condition for allowance. Upon entry of the above-made amendment, claims 1-22 and 64-74 will be pending.

Claims 1 and 12 have been amended to recite that D_{target} and $D_{\text{off-target}}$ are represented by either one of the following: (i) $D_{\text{target}} = R_{\text{target},k}(\alpha_{\text{target}}, t_l)$ and $D_{\text{off-target}} = R_{\text{off-target},k}(\alpha_{\text{off-target}}, t_l)$, respectively; (ii) $D_{\text{target}} = \sum_k \beta_k R_{\text{target},k}(\alpha_{\text{target}}, t_l)$ and $D_{\text{off-target}} = \sum_k \beta_k R_{\text{off-target},k}(\alpha_{\text{off-target}}, t_l)$, respectively; or (iii) $D_{\text{target}} = C_{\text{target}}$ and $D_{\text{off-target}} = C_{\text{off-target}}$, respectively. Support for the amendment is found in the specification at page 35, line 25, through page 36, line 25.

Claims 11, 22, and 65 have been amended to be in independent form including all of the limitations of the base claim and any intervening claims.

Claims 64 and 70 have been amended to recite that the decomposing comprises representing said drug response profile in terms of said one or a combination of pathway response profiles according to equation $D_k(t_l) \equiv \sum_i R_{i,k}(\alpha_i, t_l)$. Support for the amendment is found in the specification in Equation 5, page 26, lines 1-6.

Claim 69 has been amended to depend on claim 65.

Claims 11, 22, and 72 have also been amended to correct a typographical error.

New claim 73 has been added. Support for new claim 73 is found in the specification at, e.g., page 35, line 25, through page 36, line 25. New claim 74 has also been added. Support for new claim 74 is found in the specification at page 38, lines 1-11.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

THE REJECTION UNDER 35 U.S.C. § 103 (a)
SHOULD BE WITHDRAWN

Claims 1, 8-10, 12, 19-21, 64, 69 and 70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rine et al., U.S. Patent No. 5,777,888 ("Rine"). The Examiner maintained and reiterated the rejection from the previous office action.

A finding of obviousness under 35 U.S.C. § 103(a) requires a determination that the differences between the claimed subject matter and the prior art are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere*, 383, U.S. 1 (1956). The relevant inquiry is whether the prior art suggests the invention and whether the prior art provides one of ordinary skill in the art with a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Rine teaches systems and methods for generating and analyzing stimulated physical matrices, e.g., genome reporter matrices. The stimulated physical matrix of Rine comprises an array of units, each comprising a different responder, e.g., a gene, of a living thing or a probe corresponding to such a responder and an identifier for the responder or probe. The living thing is provided a stimulus, e.g., a drug, capable of repressing the responders of a plurality of the units and the identifiers provide physical signals corresponding to the repression of the respective responders. Rine teaches analyzing such physical matrices by comparing a stimulated physical matrix with a stimulated physical matrix database. Rine also teaches comparing the number of reporters affected by a first drug to the number of reporters affected by a second drug to determine relative specificity of the first drug to that of the second drug.

With respect to independent claims 1 and 12, Applicants respectfully submit that these claims have been amended to recited that D_{target} and $D_{\text{off}-\text{target}}$ are represented by either one of the following: (i) $D_{\text{target}} = R_{\text{target},k}(\alpha_{\text{target}}, t_l)$ and $R_{\text{off}-\text{target},k}(\alpha_{\text{off}-\text{target}}, t_l)$, respectively; (ii) $D_{\text{target}} = \sum_k \beta_k R_{\text{target},k}(\alpha_{\text{target}}, t_l)$ and $D_{\text{off}-\text{target}} = \sum_k \beta_k R_{\text{off}-\text{target},k}(\alpha_{\text{off}-\text{target}}, t_l)$, respectively; or (iii)

$D_{\text{target}} = C_{\text{target}}$ and $D_{\text{off}-\text{target}} = C_{\text{off}-\text{target}}$, respectively, where α_{target} is a scaling constant of a scaling transformation of said target pathway, $\alpha_{\text{off-target}}$ is a scaling constant of a scaling transformation of said at least one of its off-target pathway, $R_{\text{target},k}(\alpha_{\text{target}}, t_l)$ is a scaled response of cellular constituent k in said target pathway at the drug exposure level of t_l and $R_{\text{off}-\text{target},k}(\alpha_{\text{off}-\text{target}})$ is a scaled response of cellular constituent k in said at least one of its off-target pathway at the drug exposure level of t_l, β_k is a constant for cellular constituent k, C_{target} is the minimal level of said drug to achieve a threshold response in said target pathway and $C_{\text{off-target}}$ is the minimal level of said drug to achieve a threshold response in said at least one of its off-target pathways. Although Rine teaches measurement of a plurality of cellular constituents, e.g., as represented by a plurality of units of its physical matrix, Rine does not teach or suggest representing D_{target} and $D_{\text{off}-\text{target}}$ by any one of these quantities. Nor does Rine teach or suggest evaluating the specificity of a drug by comparing D_{target} and $D_{\text{off}-\text{target}}$ as represented by these quantities. A person of ordinary skill in the art would not be motivated with a reasonable expectation of success to represent D_{target} and $D_{\text{off}-\text{target}}$ in the manner as claimed in the amended claims 1 and 12, and to evaluate the specificity of a drug by comparing D_{target} and $D_{\text{off}-\text{target}}$ so represented. Therefore, Applicants respectfully submit that the invention as claimed in the amended claims 1 and 12, and the claims dependent thereon, are nonobvious under 35 U.S.C. § 103 (a) over Rine, and that the rejection of these claims under 35 U.S.C. § 103 (a) over Rine should be withdrawn.

With respect to independent claims 64 and 70, Applicants respectfully submit that these claims have been amended to recited that the decomposing comprises representing the drug response profile in terms of the one or a combination of pathway response profiles according to equation

$$D_k(t_l) \equiv \sum_i R_{i,k}(\alpha_i, t_l)$$

wherein t_l is a level of the drug, α_i is a scaling constant of a scaling transformation of pathway i, $D_k(t_l)$ is the measurement of cellular constituent k in said drug response profile at the drug exposure level of t_l, $R_{i,k}(\alpha_i, t_l)$ is the measurement of cellular constituent k in pathway i at the drug exposure level of t_l. Rine does not teach or suggest decomposing a drug response profile into one or a combination of pathway response profiles as claimed. Nor does Rine teach or suggest evaluating specificity of the drug by comparing, among the one or a combination of pathway response profiles, the pathway response profiles for the one or more biological pathways associated with therapeutic effects of the drug with the pathway response profiles for the one or more biological pathways that are associated with one or more non-therapeutic effects of the drug. A person of ordinary skill in the art would not be motivated with a reasonable expectation of success to decompose a drug response profile as claimed in the amended claims 64 and 70. Thus, Applicants respectfully submit that the invention as claimed in the amended claims 64 and 70, and the claims dependent thereon, are nonobvious under 35 U.S.C. § 103 (a) over Rine, and that the rejection of these claims under 35 U.S.C. § 103 (a) over Rine should be withdrawn.

THE OBJECTION TO CLAIMS 11, 22, 65-68, 71 and 72 SHOULD BE WITHDRAWN

Claims 11, 22, 65-68, 71 and 72 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants have amended these claims to be in independent form including all of the limitations of the base claim and any intervening claims. Therefore, the objection to claim 11, 22, 65-68, 71 and 72 is obviated and should be withdrawn.

CLAIMS WITHDRAWN FROM CONSIDERATION AS BELONGING TO NON-ELECTED SPECIES SHOULD BE CONSIDERED

Claims 2-7 and 13-21 were withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claims are allowable, claims 2-7 and 13-21 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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